# Brain Metastasis and Leptomeningeal Carcinomatosis in a Patient With Cholangiocarcinoma

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## CASE REPORT

A 51-year-old white man was diagnosed with intrahepatic cholangiocarcinoma in March 2009. He initially presented with right upper quadrant pain and jaundice. He was found to have a large mass replacing the left lobe of the liver, with extension to the right lobe of the liver. Histopathologic analysis revealed adenocarcinoma, and tumor cells were strongly positive for CK7 and negative for CK20, PSA, chromogranin, synaptophysin, COX-2, TTF-1, and Hep-Par. The results were suggestive of carcinoma of pancreatic-biliary origin. A positron emission-computed tomography scan showed increased glucose uptake in the liver along with increased uptake in a left pericardiophrenic lymph node and left parahilar lymph node.

He received systemic therapy with fixed-dose rate gemcitabine followed by oxaliplatin starting in April 2009.[1] He initially responded to therapy, but restaging scans after 12 cycles (24 weeks) revealed disease progression with increasing size of periaortic lymphadenopathy, peritoneal nodules, and mediastinal adenopathy. He then received irinotecan with leucovorin-modulated bolus 5-flourouracil (5-FU) followed by a 46-hr infusion of 5-FU starting September 2009. Restaging scans after 4 cycles (8 weeks) of therapy revealed disease progression with increasing size of mediastinal lymph nodes, and interval enlargement of a large left hepatic mass with new adjacent satellite nodules. He next received mitomycin C in combination with oral capecitabine on a 4-week schedule starting early December 1, 2009.[2] Cycle 2 began on December 29, 2009.

He presented January 4, 2010, with altered mental status that got progressively worse over the prior 3–5 days. Physical examination was grossly unremarkable. A detailed neurologic exam was not possible because of the patient's inability to cooperate, yet a subtle weakness was noted on the left side of the body. Laboratory studies were unremarkable except for mild elevation of alkaline phosphatase at 170 U/L and total bilirubin of 1.6 mg/dL. A CT scan of the brain performed without contrast showed a 1.4 cm left parietal isodense lesion with surrounding brain edema.

The patient's level of consciousness improved significantly over the next couple of days with intravenous dexamethasone 4 mg every 6 hr. Magnetic resonance imaging scan of the brain revealed 2 small enhancing cerebral cortical nodules and abnormal cerebrospinal fluid and extensive leptomeningeal enhancement suggestive of metastatic carcinomatosis (Figure 1). A lumbar puncture was performed that showed a normal opening pressure; the cerebrospinal fluid was clear. Chemical analysis of the fluid revealed a protein of 91 mg/dL, glucose of 50 mg/dL, and 128 white blood cells per cubic millimeter, of which 21% were adenocarcinoma cells, confirming the diagnosis of leptomeningeal carcinomatosis. The patient received 1 dose of 300 cGy radiation to the whole brain, but he and his family elected to discontinue therapy and was discharged to home hospice care. He died on January 21, 2010.

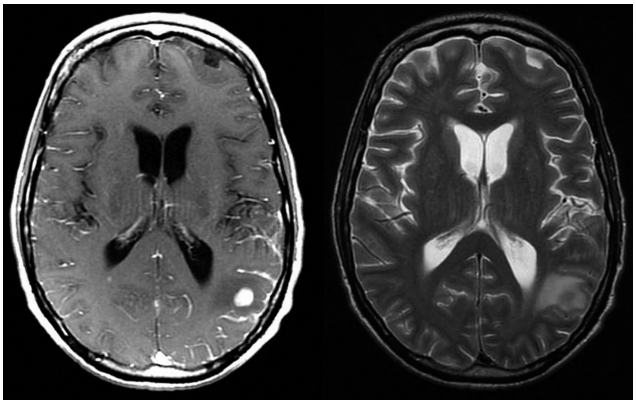

**Figure 1.** MRI of the brain showing an enhancing left parietal nodule along with diffuse meningeal enhancement.

## DISCUSSION

Cholangiocarcinomas (CCs) are malignant tumors arising from the epithelial cells lining the biliary tree. Despite several advances in the diagnosis and therapy of CCs, the prognosis remains dismal for most patients because the majority present with advanced stage and are not candidates for curative resection.[3–4] Median survival for patients with metastatic disease is generally less than 1 year. CCs typically invade the liver parenchyma, portal ducts, and portal vein and spread via lymphatics to regional lymph nodes. Hematogenous spread to distant organs may also occur. Brain metastasis and leptomeningeal carcinomatosis secondary to cholangiocarcinoma is exceedingly rare, with only a few cases reported in the literature.[5–7] We report another case of this rare, and fatal, complication of CC.

The arachnoid membrane and pia mater comprise the leptomeninges. The subarachnoid space containing the cerebrospinal fluid (CSF) separates the arachnoid membrane and the pia mater. Neoplastic infiltration of the leptomeninges may occur either by lymphatic or hematogenous spread or by direct extension from a tumor.[8–12] The malignant cells migrate through the arachnoid vessels or choroid plexus to the surrounding adventitia to gain entry to the CSF.

Symptomatic involvement of the leptomeninges is recognized clinically in 4–7% of all cancer patients.[8–12] Asymptomatic involvement, detected at autopsy, averages 20% and may be higher for certain cancers. The most common nonhematologic tumors associ-

ated with leptomeningeal metastases are breast cancer, lung cancer, and melanoma. In our case, the tumor spread to the leptomeninges may have been due to spread from intraparenchymal brain metastasis. Leptomeningeal carcinomatosis confers a poor overall prognosis, with mean survival from the time of diagnosis of 2–4 months.

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### Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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